Design, Synthesis and Structural Analysis of New Macrocycles Containing Dispiro-1,3-dioxane Units

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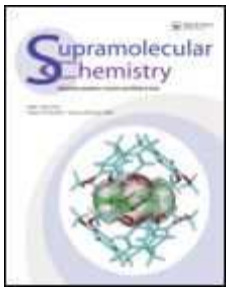

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Design, Synthesis and Structural Analysis of New Macrocycles Containing Dispiro-1,3-dioxane Units

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Keywords:	macrocycles, crystal structure, dynamic NMR, dispiranes, 1,3-dioxanes

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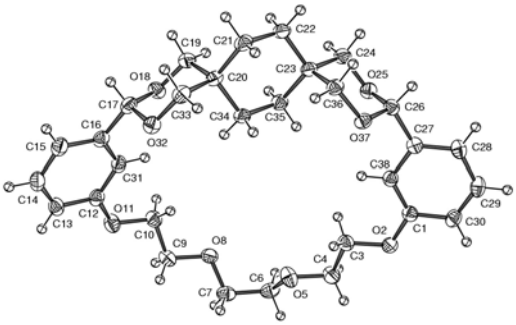

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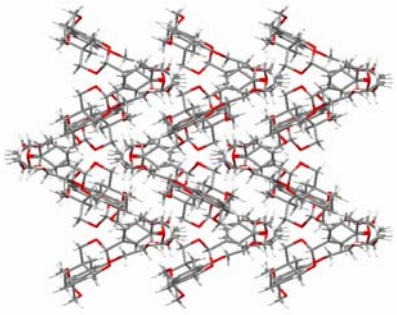
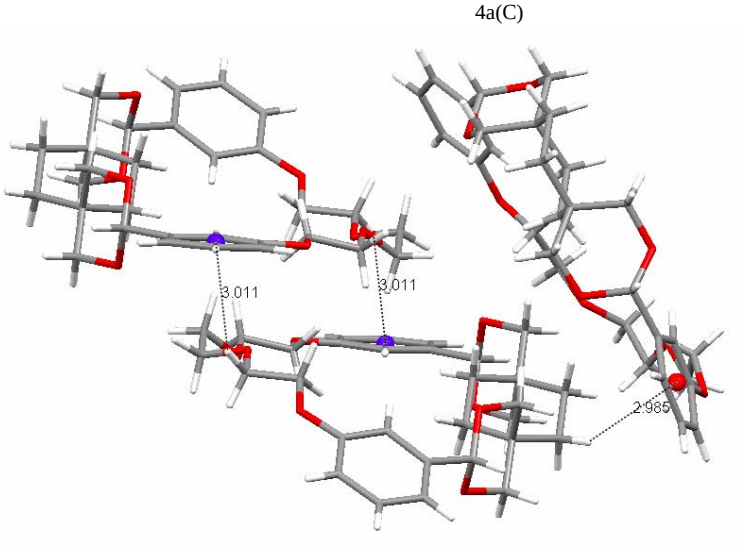


4a(A)

c



4a(C)

4a(B)

b

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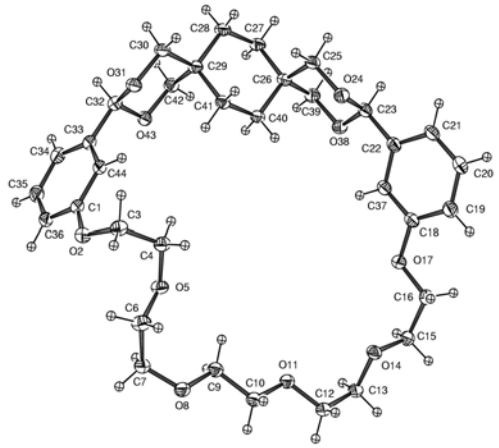
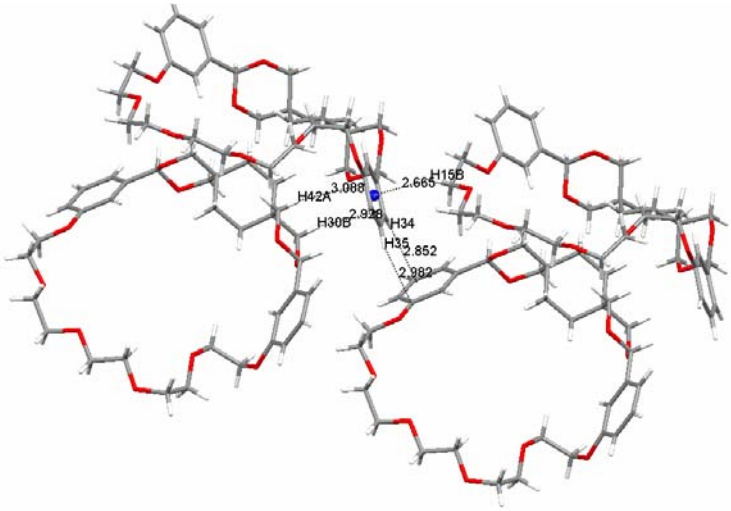


a



b

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Design, Synthesis and Structural Analysis of New Macrocycles Containing Dispiro-1,3-dioxane Units

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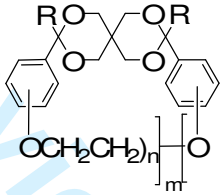
The synthesis and the structure of new macrocycles containing semiflexible dispiro-1,3-dioxane units is reported. The structural analysis of the compounds is performed by high field NMR spectra, mass spectrometry investigations (MALDI, ESI-MS) and the solid state molecular structure obtained for two compounds by single crystal X-ray diffractometry. The dynamics of the macrocycles promoted by the flipping of the middle cyclohexane ring of the dispirane units is investigated using low temperature NMR experiments

Keywords: Macrocycles, Crystal structure, Dynamic NMR, Dispiranes, 1,3-Dioxanes

INTRODUCTION

The synthesis and structural analysis of macrocyclic compounds as "hosts" for cations, anions and organic molecules is an important target in organic chemistry.[1-22] Relevant features in high yield macrocyclisation reactions are the geometry of the substrate, which has to exhibit the pre-organization[23,24] required by the incorporation in the macrocycle, and the high number of heteroatoms of the reacting compounds, which can coordinate to cations and promote the macrocyclisation by *template* effect.[25,26] Many papers [27-37] deal with macrocycles that embed in their structure saturated oxygenated heterocycles pertaining to sugars, spiranes or bicycles. Recently,[38,39] we reported the synthesis, structural analysis, and complexation ability of new macrocycles containing anancomeric spiro-1,3-dioxane units (I, Scheme 1).



R = H, CH_3

n = 1-6; m = 1-4 I

meta, para

SCHEME 1. Macrocycles with monospirane units

The synthesis of these derivatives was carried out in good yields, in high dilution or in *template* procedures and the reactions underwent with the obtaining of mixtures of monomers, dimers, trimers and tetramers. The NMR, X-ray diffractometry and mass spectrometry (MALDI, FAB and ESI-MS) supported structural analysis of the separated terms pointed out the "rigid" (anancomeric) conformational behavior of the spirane units, the intra and intermolecular π-stacking and the chemoselective ability of these macrocycles as hosts for cations and solvent molecules.

The investigations[40,41] on the stereochemistry of substituted dispiranes with six-membered rings **1** showed separable *syn* and *anti* isomers (II-IV, Scheme 2). The *syn* structures (II and III) are chiral being built up by merging two monospirane units with similar configurations (AB and BC monospirane units are of M configuration for II and of P configuration for III). The *anti* structure is achiral and the merged monospirane units (AB and

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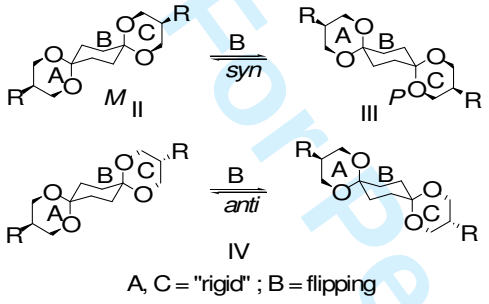
BC) display different configurations. Dispiranes **1** have semiflexible structure. The peripheral substituted 1,3-dioxane rings are "rigid", while the middle carbocycle is flipping. The conformational equilibrium is enantiomeric inversion for *syn* isomer and the conformational equilibrium of the centrosymmetric *anti* isomer occurs between two equivalent structures (homomeric equilibrium). The patterns of the ^{1}H-NMR spectra (*rt*) for the protons of ring B are very different for *syn* (two singlets) and *anti* structures (multiplets according to an AA'BB' system) and the discrimination of these isomers and the determination of their ratio in mixtures of isomers are easily carried out by NMR.



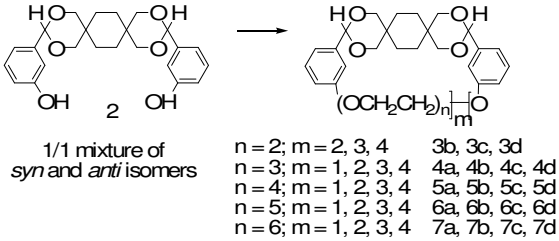
SCHEME 2. Conformational equilibria for semiflexible dispiro-1,3-dioxanes

In order to develop the investigations of the host molecules with (poly)spirane units we designed new macrocycles which incorporate semiflexible dispirane units and we planed to study the reactivity of *syn* and *anti* isomers of dispiranes in the macrocyclisation reaction, and the influence of the semiflexible conformational behavior of the dispirane units on the structure and proprieties of the target macrocycles. The geometry of *syn* isomers is favorable to the macrocyclisation, while the reacting groups located at the extremities of the dispirane exhibit opposite orientations in the *anti* isomers and the macrocyclisation is expected to be difficult in this case.

RESULTS AND DISCUSSIONS

New macrocycles (**3**-**7**), containing dispiro-1,3-dioxane units, were obtained by the *template* reaction of dispirane **2** with several ditosylated polyethyleneglycols. The reactions were performed starting from the 1/1 mixture of *syn* and *anti* isomers of dispirane **2** (obtained from 1,1,4,4-tetrahydroxymethylcyclohexane[42,43] and *meta*-hydroxybenzaldehyde), in acetonitril, and using Cs_2CO_3 as base and as *template* (Scheme 3; Table 1).

The mixture of isomers of **2** was used as substrate, on the one hand, because all the attempts to separate the *syn* and *anti* isomers by column chromatography or by crystallization failed (mainly because both isomers have a very low solubility in usual solvents) and on the other hand because we expected the high differences of reactivity between *syn* and *anti* isomers in the macrocyclisation reaction. The mass spectrometry investigations (MALDI, ESI-MS) of crude products showed the formation of monomers and oligomers (from dimers to tetramers) and the NMR spectra revealed important amounts of unreacted *anti* isomer of **2**. The monomers are obtained only for **4**-**7** and only the *syn* isomer of **2** participates to their formation. The synthesis of **4-7** also leads to dimers and small amounts of higher terms (trimers and tetramers).



SCHEME 3. Synthesis of macrocycles with dispiro-1,3-dioxane units

TABLE 1. Results of the synthesis of compounds **3-7**

Compound	n	Yields in monomer (%)*	Yields in dimers, trimers and tetramers#
3	2	-	61
4	3	28	34
5	4	32	43
6	5	28	50
7	6	20	11

*Calculated taken into account only the amount of *syn* isomer
#Calculated for the mixture of dimers, trimers and tetramers and considering the amount of mixture of *syn* and *anti* isomers

These larger macrocycles are obtained by the cyclisation reaction of both *syn* and *anti* isomers, with the major participation of the *anti* isomer of **2**. For **3** the main products are the dimers and the trimers.

The mixtures of oligomers (from dimers to tetramers) and isomers of **3** and **7** were subjected to separation (discrimination) by HPLC using a C^{18} column and water/methanol = 1/4 as elution system. The chromatograms showed high values of the ratios dimers/trimers (**3b/3c**: 3.5/1 and **7b/7c**: 6/1) and dimers/tetramers (**7b/7d**: 19/1). The *anti-anti* (rt = 23.45 min) and the *syn-anti* (rt = 22.03 min) dimers of **7b** (ratio 1/1) could be separated by semipreparative HPLC [the formation of the third possible isomer (*syn-syn*) was not observed]. Only the *syn-syn* isomer of dimers of **3** could be separated after several crystallizations from the mixture of *syn-syn*, *syn-anti* and *anti-anti* isomers (7/7/1 ratio; determined from the NMR spectrum of the fraction of dimers separated by HPLC). Four isomers are possible for **7c** (*anti-anti-anti, syn-anti-anti*, *syn-syn-anti* and *syn-syn-syn*). Two fractions with trimers (rt_1 = 30.96 min., rt_2 = 32.09 min in the

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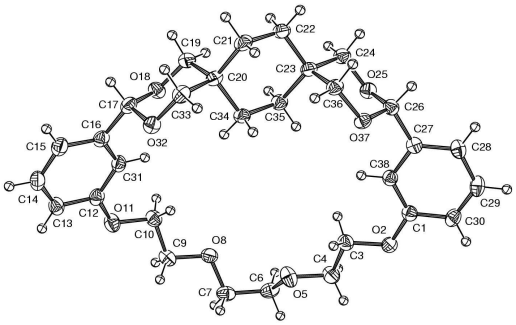
ratio 20/1) were separated (HPLC) for **7c**. The NMR spectra showed that the main fraction contains the 1/1 mixture of *anti-anti-anti* and *syn-anti-anti* isomers, while the second fraction mainly exhibits the *syn-syn-anti* isomer. The formation of the fourth possible trimer could not be observed. The *anti-anti* dimer of **4b** was isolated by column chromatography (toluene/acetone/ethyl acetate: 4/1/0.5). All the attempts to obtain other pure dimers or trimers failed.

Structural aspects in solid state

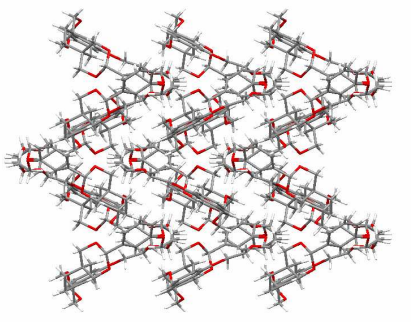
The molecular structures of two monomers (**4a** and **6a**) were obtained by X-ray diffractometry. The ORTEP diagrams (Figures 1a and 2a) show the *syn* orientation of the 1,3-dioxane rings (referred to the central cyclohexane), the equatorial orientation of the aromatic rings located at the extremities of the dispirane skeleton and their peculiar rotameric behavior (intermediary to the usual bisectional [$\alpha(\beta) = 0°$] and orthogonal [$\alpha(\beta) = 90°$] rotamers). The values of the angles between the aromatic rings and the best planes of the 1,3-dioxane rings for **4a** [$\alpha(C^{12}C^{13}C^{14}C^{15}C^{16}C^{31}$ / $C^{21}C^{20}C^{34}) = 33.07°$; $\beta(C^{1}C^{27}C^{28}C^{29}C^{30}C^{38}$ / $C^{22}C^{23}C^{35}) = 5.56°$] and for **6a** [$\alpha$ ($C^{1}C^{33}C^{34}C^{35}C^{36}C^{44}$ / $C^{28}C^{29}C^{41}) = 36.18°$; β ($C^{18}C^{19}C^{20}C^{21}C^{22}C^{37}$ / $C^{27}C^{26}C^{40}) = 35.41°$] show a closer disposition to the bisectional rotamer.

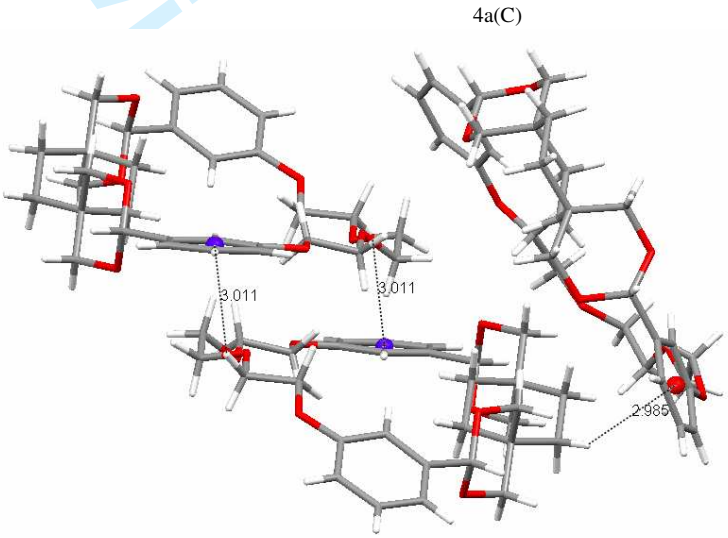
The investigations of the lattices showed significant intermolecular C-H - π interactions between the aromatic rings and the hydrogen atoms of the cyclohexane or of the ethylene oxide units. In the lattice of **4a** the formation of dimers [Figure 1b; molecules **4a**(A) and **4a**(B)] due to C-H – π interactions of the aromatic rings $C^{1}C^{27}C^{28}C^{29}C^{30}C^{38}$ with one of the hydrogen atom at C^{9} (ethylene oxide chain) is observed. The distance from this hydrogen atom to the plane of the aromatic ring is 2.94 Å. Each dimer unit exhibits other four C-H – π interactions with other four dimer units. These interactions involve the $C^{12}C^{13}C^{14}C^{15}C^{16}C^{3}$ type aromatic rings and the equatorial hydrogen atom at C^{21} (its distance to the plane of the aromatic ring is 2.85 Å) pertaining to the cyclohexane moieties [only one interaction with molecule **4a**(C) is shown in Figure 1b]. The view along the c crystallographic axis reveals the interesting *zigzag* arrangement of the molecules (Figure 1c) The lattice of **6a** (Figure 2b) shows the *edge-tilted-to-face* arrangement of the different types of aromatic rings pertaining to neighboring molecules. The dihedral angle between these aromatic rings is 83.05°; the distance between the centers of the aromatic rings is 5.27 Å and the distances from H^{34} and H^{35} to the plane of the other aromatic ring ($C^{18}C^{19}C^{20}C^{21}C^{22}C^{37}$) are 2.85 and 2.98 Å, respectively.



a

4a(A)

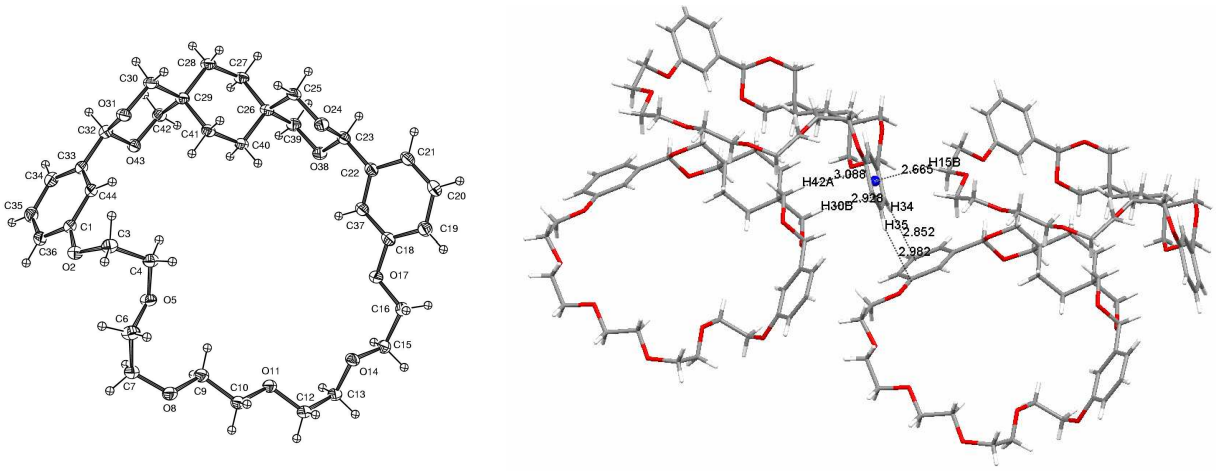




4a(B)

b

FIGURE 1. Single c tal molecular structure of **4a**: ORTEP diagram (a), Mercury representatio.. .. a part of the lattice showing the acteristic CH-π interactions (b) and view of the lattice along the c crystallographic axis (c)



a b

FIGURE 2. Single crystal molecular structure of **6a**: ORTEP diagram (a) and Mercury representation of a part of the lattice showing the characteristic CH-π interactions (b).

The short distance between the centroid of the aromatic ring $C^1C^{33}C^{34}C^{35}C^{36}C^{44}$ and the hydrogen atom at position 15 of a third molecule (d = 2.66 Å) reflects other important stacking interactions. The same aromatic ring $C^1C^{33}C^{34}C^{35}C^{36}C^{44}$ is involves in weaker C-H - π interactions with the axial hydrogen atoms at positions 30 (distance to the aromatic plane, d = 2.92 Å) and 42 (distance to the aromatic plane, d = 3.08 Å) of a fourth molecule of macrocycle of the lattice.

Structural aspects in solution

The NMR investigations of the monomers and dimers at *rt* (Table 2) show the semiflexible behavior of the dispirane units, with anancomeric 1,3-dioxane rings and flipping cyclohexane units. In ^{1}H NMR spectra, the protons of the 1,3-dioxane rings exhibit different signals (doublets) for the axial and equatorial positions, while the signals of the protons of the cyclohexane ring are two singlets for *syn* structures and two multiplets for the *anti* units.

The conformational equilibria of the monomers with *syn* dispirane units represent enantiomeric inversions [V (M) ⇆ VI (P); Scheme 4]. These conformational processes were investigated using variable temperature ^{1}H NMR experiments run with compound **4a** (Figure 3).

The *rt* spectrum (toluene-d_8, 600 MHz) exhibits a doublet for the axial protons of the 1,3-dioxane ring (δ_{ax}= 3.15 ppm) and another doublet for the equatorial protons of the same positions (δ_{eq}= 3.70 ppm), while the protons of the cyclohexane moiety show two singlets (δ = 0.58 , δ' = 2.04 ppm). The protons of the three ethylene oxide units exhibit 2 multiplets (δ = 4.06, δ' = 3.54 ppm) and a singlet (δ = 3.32 ppm). Lowering the temperature coalescences are observed, and the spectrum at 190 K shows the frozen structure of the compound. In the frozen structure, the CH_2 groups of the 1,3-dioxane are not rendered equivalent anymore by the flipping of the cyclohexane ring. One of these groups is axial and the other one is equatorial with respect to the middle cyclohexane ring and they exhibit different signals in the low temperature NMR spectrum. The low temperature spectrum of **4a** is significantly more complex.

Table 2. NMR data (600 MHz, δ, ppm) for compounds 3b, 4a-7a, 4b, 6b and 7b

Compd.	Solv.	1,3-Dioxane units		Cyclohexane units			
		eq.	ax.	*Syn**		*Anti***	
3b (*syn-syn*)#	$CDCl_3$	4.04	3.55	1.96	1.12	-	-
4a	Tol.-*d*8	3.70	3.14	2.05	0.59	-	-
4b (*anti-anti*)	$CDCl_3$	3.99	3.56	-	-	1.76	1.22
5a	C_6D_6	3.73	3.15	1.92	0.50	-	-
6a	$CDCl_3$	4.07	3.59	2.09	1.14	-	-
7a	C_6D_6	3.75	3.15	1.89	0.48	-	-
7b (*anti-anti*) §	CD_2Cl_2	3.99	3.57	-	-	1.76	1.23
7b (*syn-anti*) §	THF-d*8*	4.00	3.51	1.89	1.07	1.76	1.20

* singlets, **multiplets, #500 MHz, §400 MHz

The assignment of the signals is not possible, but it can be observed that the two doublets recorded at *rt* for the protons of the 1,3-dioxane moieties and the two triplets recorded for the protons of the bordering ethylene oxide groups are replaced in the low temperature NMR spectrum by 8 groups of signals in the range 3.0-4.2 ppm

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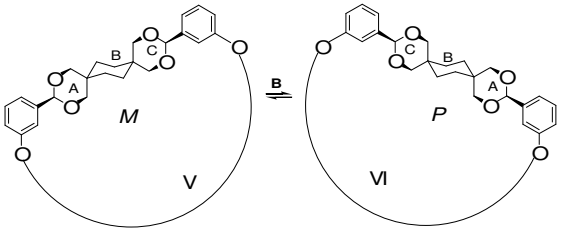


SCHEME 4. Conformational equilibrium for monomers **4a**-**7a**

The flipping of the cyclohexane rings of the *anti* units in the *anti-anti* dimers (Scheme 5; VII⇆VIII) or of the *syn* units in the *syn-syn* dimer of **3** (simplified representation in Scheme 6; IX⇆X⇆XI) are diastereoisomeric equilibria.

The chains of the *anti-anti* dimer macrocycle (Scheme 5) can connect terminal monospirane units with the same configuration in diastereoisomer VIII or of different configurations in diastereoisomer VII. For these dimers (VII and VIII, *anti-anti* structures) we can consider that the macrocycle exhibits four similar chiral elements (as constitution and as configurations). The possible diastereoisomers are generated by the different positions in the cycle of the chiral elements with the same configurations and they belong to the family of cyclostereoisomers, being cyclodiastereoisomers[44] (Scheme 5).

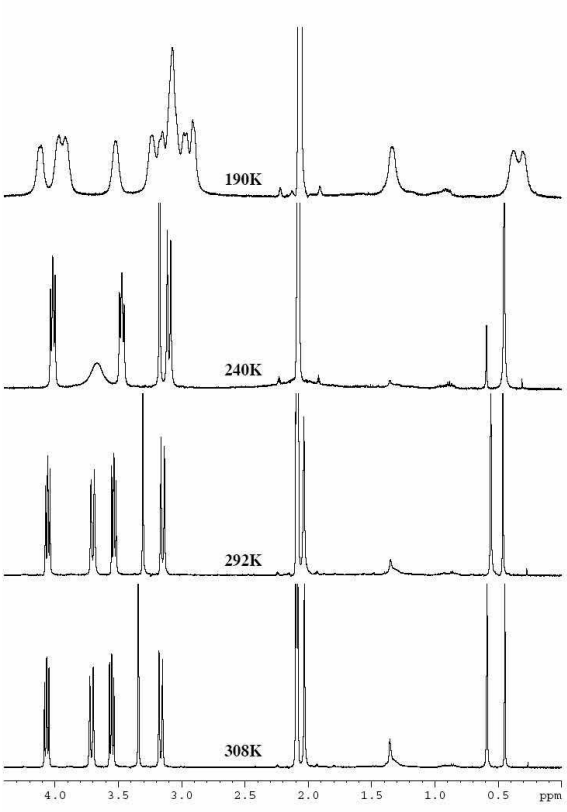
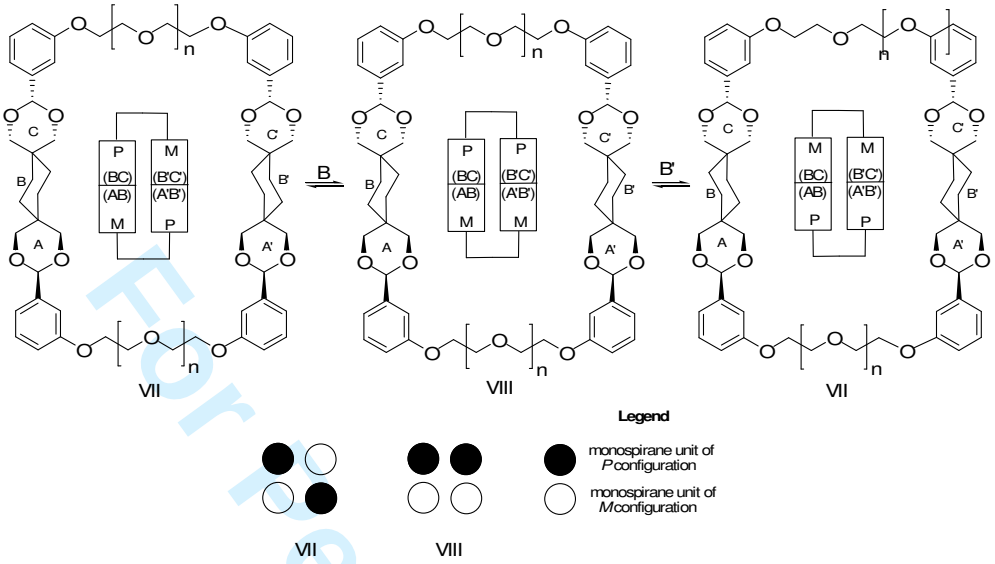


FIGURE 3. Variable NMR spectra run with compound **4a**.

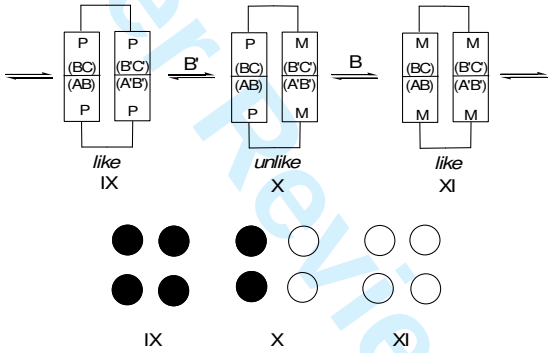
The flipping of one of the cyclohexane rings (B or B') transforms one diastereoisomer into the other. The flipping of the middle ring in the *syn-syn* dimer **3b** equilibrates *like* (IX, XI) and *unlike* (X) structures (Scheme 6).

The variable temperature ^{1}H NMR experiments (CD_2Cl_2) performed with the *anti-anti* isomer of **7b** showed important modifications of the signals pertaining to the methylene protons of the 1,3-dioxane rings and of those of the cyclohexane rings. At *rt* the spectrum exhibits two doublets (δ_{eq} = 3.99 and δ_{ax} = 3.57 ppm) for the protons of the 1,3-dioxane rings and two multiplets (δ = 1.23 and δ' = 1.76 ppm) for the protons of the cyclohexane rings. At low temperature the spectra of the frozen structure are complicated because they exhibit the signals of two frozen diastereoisomers (VII and VIII) and because the CH_2 groups of the same 1,3-dioxane cycle are not equivalent anymore (one of the groups is equatorial and the other one is axial as referred to the neighboring cycle). The signals of the dispirane units begin to modify at 250 K and at 220 K they are

practically completely incorporated in the base line. The signals reappear (at different chemical shifts) at 200 K and at 190 K (the lowest temperature reached in this experiment) and one can observe two groups of signals (unsolved) for the protons of the 1,3-dioxane rings in the ranges 3.4-3.7 ppm and 4.2-4.3 ppm and other two groups of signals in the ranges 0.8-1.05 ppm and 2.15-2.2 ppm for the protons of the cyclohexane rings



SCHEME 5. Conformational equilibria involving the cyclodiastereoisomers of the *anti-anti* dimers.



SCHEME 6. Representation of the conformational equilibria involving the *like* and *unlike* diastereoisomers of the *syn-syn* dimers.

CONCLUSIONS

The synthesis of macrocycles containing dispiro-1,3-dioxane units was carried out starting from dispiranes with phenol groups and from ditosylated polyethylene glycols. The monomers were obtained only by the enclosure in the macrocycles of the *syn* dispirane isomers, while the higher terms (dimers, trimers….) were obtained with the participation of both *syn* and *anti* dispiranes. The structural analysis using variable temperature NMR experiments revealed the flipping of the central cyclohexane ring of the dispirane units inside the macrocycle having as result enantiomeric inversions for monomers and diastereoisomeric equilibria for dimers.

EXPERIMENTAL PART

NMR spectra [^{1}H (600, 500 or 400 MHz), ^{13}C (150, 125, or 100 MHz), COSY, APT, HETCOR (HMBC, HMQC), NOESY or ROESY] were recorded at rt, in $CDCl_3$, C_6D_6, Tol.-d_8, CD_2Cl_2, THF-d_8. Melting points are uncorrected. Microanalyses (C, H) agreed with calculated data. FAB and MALDI$^+$ spectra were obtained on a JEOL JMS AX-500 spectrometer under usual conditions. X-ray crystallographic data for **4a** and **6a** are deposited CCDC-239963(**4a**) and CCDC-255760 (**6a**) at Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat. +44-1223/336-003; e-mail: deposit@ccdc.cam.ac.uk and they can be obtained free of charge at http:// www.ccdc.cam.ac.uk/conts/retrieving.html.

The structural (crystallographic) data were collected on a NONIUS Kappa CCD diffractometer with graphite monochromatized MoK_α radiation.[45] The cell parameters are obtained with *Denzo* and *Scalepack*[46] with 10 frames (ψ rotation : 1° per

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frame). The structure was solved with SIR-97[47] which reveals the non hydrogen atoms of the compounds. After anisotropic refinement, many hydrogen atoms may be found with a Fourier Difference. The whole structure was refined with SHELXL97[48] by the full-matrix least-square techniques. Atomic scattering factors from International Tables for X-ray Crystallography.[49] Ortep views realized with PLATON98.[50] The parameters of the crystals and of the determinations are given in Table 3.

TABLE 3. Details of the X-ray diffractometry molecular structure determinations.

Parameters\compound	**4a**	**6a**
Empirical formula	$C_{30}H_{38}O_8$	$C_{34}H_{46}O_{10}$
Formula weight	526.60	614.71
Temperture (K)	130	120(1)
Wavelength (Å)	0.71069	0.71069
Crystal system	orthorhombic	monoclinic
Space group	Pbca	P21/a
Unit cell dimensions		
a (Å)	16.0200(2)	12.0158(3)
b (Å)	12.1790(1)	18.5170(4)
c (Å)	28.1491(3)	15.0221(3)
α (°)	90	90
β (°)	90	109.3560(10)
γ (°)	90	90
Volume (Å^3)	5492.1(1)	3153.45(12)
Z	8	4
Density (calc.) (mg/m $^{-3}$)	1.274	1.295
Absorption coefficient (mm^{-1})	0.092	0.094
F(000)	2256	1320
Crystal size(mm)	0.45∗0.32∗0.30 mm	0.35 x 0.35 x 0.08 mm
Reflections collected	6284	7210
Independent reflections	6284 [R(int) = 0.0000]	7210 [R(int) = 0.0000]
Reflections observed	4641	5774
Data / restraints / parameters	6284 / 0 / 344	7210 / 0 / 398
Final R indices [$F^2>2\sigma(F^2)$]	R_1= 0.0475 wR_2 = 0.1330	R_1 = 0.0499 wR_2= 0.1297
R indices (all data)	R_1 = 0.0716 wR_2= 0.1530	R_1 = 0.0655 wR_2 = 0.1429

Analytical HPLC was performed on a Thermo Separation Products (Courtaboeuf, France) P4000 Liquid Chromatograph pump coupled to a Thermo Separation Products (Courtaboeuf, France) UV 200 detector. Data were collected by Chromquest 2.51 software from Thermoquest Corporation. Analytical column was a HyPURITY® Cl8 (125 mm × 4 mm; 5 µm) purchased from Thermo Hypersil (Courtaboeuf, France). Semi-preparative purification was performed on a Varian 9010 HPLC pump coupled to a Varian 9050 UV detector. The chromatographic column was a Nucleosil C18 (250 mm × 10 mm; 5 µm) from Interchim (Monluçon, France). Separations were carried out at room temperature in gradient elution mode (H_2O:MeOH 20:80 to 0:100 in 30 min) at 4 mL/min. Solutions of crude mixture were prepared in THF at a concentration of 5 g/L for analytical chromatography and 50 g/L for semi-preparative chromatography. The fractions collected by semi-preparative chromatography were evaporated to dryness under vacuum. All solvents were of HPLC grade and were purchased from VWR (Fontenay-sous-Bois, France).

Procedure for the synthesis of 2

The *meta*-hydroxybenzaldehyde (44 mmol) and 0.2 g of *p*-toluenesulphonic acid were added to a solution of 15 mmol 1,1,4,4-tetrahydroxymethylcyclohexane in 200 ml toluene. The mixture was refluxed and the water resulting from the reaction was removed using a Dean-Stark trap. After the theoretical amount of water was separated, the reaction mixture was cooled at room temperature and the catalyst was neutralized (under stirring) with powdered CH_3COONa in excess (0.4g). The reaction mixture was washed twice with 100 ml water. The organic layer was dried over Na_2SO_4, then the toluene was removed under reduced pressure and the crude dispiro compound was subjected to flash chromatography (pentane/acetone = 3/1).

General procedure for the synthesis of 3-7

Dispirane **2** (4.8 mmol) and 24 mmol Cs_2CO_3 in 0.9 l acetonitrile have been refluxed for 12 h. To the obtained suspension, under refluxing solvent, 4.8 mmol of ditosylated polyethyleneglycol dissolved in 0.1 l acetonitrile have been added during 4 days using a syringe pump. The reflux of the solvent has been continued for one more day. The system was brought to rt and the solid phase was removed by filtration. The acetonitrile was evaporated and the crude product was dissolved in 300 ml CH_2Cl_2 and then washed with 2x100 ml solution of KOH 2% and 2x100 ml of water. After drying (Na_2SO_4) the solvent was removed and the crude product was subjected to flash chromatography.

2,5,8,15,22,29,32,35,42,49,56,61,64,69-tetradeca oxaundecacyclo[49.3.$2^{14,17}$.$2^{17,20}$.$2^{20,23}$.$2^{41,44}$.$2^{44,47}$.$2^{47,50}$.$1^{1,51}$.$1^{9,13}$.$1^{24,28}$.$1^{36,40}$]heptaconta-9,11,24,26,36, 38,51,53,1(70),55,62,63-dodecaene (3b). White solid, mp 254-256 ºC, several crystallisation from ethylacetate, 16.0% yield. δ_H (500 MHz, $CDCl_3$) 1.12, 1.96 (s, 16H, 18-H, 19-H, 45-H, 46-H, 58-H, 59-H, 66-H, 67-H), 3.55 (d, *J*=11.3 Hz, 8H, 16-H_{ax}, 21-H_{ax}, 43-H_{ax}, 48-H_{ax}, 57-H_{ax}, 60-H_{ax}, 65-H_{ax}, 68-H_{ax}), 3.92 (t, *J*=4.9 Hz, 8H, 4-H, 6-H, 31-H, 33-H), 4.04 (d, *J*=11.3 Hz, 8H, 16-H_{eq}, 21-H_{eq}, 43-H_{eq}, 48-H_{eq}, 57-H_{eq}, 60-H_{eq}, 65-H_{eq}, 68-H_{eq}), 4.18 (t, *J*=4.9 Hz, 3-H, 7-H, 30-H, 34-H), 5.37 (s, 14-H, 23-H, 41-H, 50-H), 6.90 (dd, *J*=8.2, 2.7 Hz, 4H, 10-H, 27-H, 37-H, 54-H), 6.98 (d, *J*=7.5 Hz, 4H, 11-H, 26-H, 38-H, 53-H), 7.17 (overlapped peaks, 4H, 12-H, 25-H,

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39-H, 52-H), 7.24 (overlapped peaks, 4H, 55-H, 62-H, 63-H, 70-H); δ_C (125 MHz, $CDCl_3$) 25.93, 26.67 (18-C, 19-C, 45-C, 46-C, 58-C, 59-C, 67-C, 66-C), 32.87 (17-C, 20-C, 44-C, 47-C), 67.95 (3-C, 7-C, 30-C, 34-C), 70.22 (4-C, 6-C, 31-C, 33-C), 75.42 (16-C, 21-C, 43-C, 48-C, 57-C, 60-C, 65-C, 68-C), 102.08 (14-C, 23-C, 41-C, 50-C), 112.16 (55-C, 62-C, 63-C, 70-C), 116.09 (10-C, 27-C, 37-C, 54-C), 119.38 (11-C, 26-C, 38-C, 53-C), 129.33 (12-C, 25-C, 39-C, 52-C),140.18 (13-C,24-C, 40-C, 51-C), 159.28 (1-C, 9-C, 28-C, 36-C). FD^+ : m/z: 965.7 $[M+H]^+$. $C_{56}H_{68}O_{14}$ requires: C, 69.69; H, 7.10%: found: C, 69.51; H, 7.27%.

2,5,8,11,18,25,32,37-octaoxahexacyclo[25.3.2^{17,20}.2^{20,23}.2^{23,26}.1^{1,27}.1^{12,16}]octatriaconta-1(38),12,14,16(31),27,29-hexaene (4a). White solid, mp 194.5-195 ºC, column chromatography, (dichloromethane/pentane/ethylacetate =4/1/0.5; R_f=0.29) 14.0% yield. δ_H (600 MHz, Tol-*d*8) 0.15 (s, 4H, 21-H, 22-H), 2.13 (s, 4H, 34-H, 35-H), 3.28 (d, *J*=10.8 Hz, 4H, 19-H_{ax}, 24-H_{ax}, 33-H_{ax}, 36-H_{ax}) 3.33 (s, 4H, 6-H, 7-H,) 3.55 (t, *J*=7.2 Hz, 4H, 4-H, 9-H) 3.71 (d, *J*=10.8 Hz, 4H, 19-H_{eq}, 24-H_{eq}, 36-H_{eq}, 33-H_{eq}) 4.13 (t, *J*=7.2 Hz, 4H, 3-H, 10-H) 5.32 (s, 2H, 17-H, 26-H) 6.83 (overlapped peaks, 2H, 15-H, 28-H), 6.92 (overlapped peaks, 2H, 13-H, 30-H), 7.15 (overlapped peaks, 2H, 14-H, 29-H) 7.69 (overlapped peaks, 2H, 31-H, 38-H); δ_C (150 MHz, Tol-*d*8) 25.74 (21-C, 22-C) 25.76 (34-C, 35-C), 33.14 (20-C, 23-C), 66.48 (3-C, 10-C), 69.05 (4-C, 9-C) 70.96 (6-C, 7-C) 74.47 (19-C, 24-C, 36-C, 33-C) 102.16 (17-C, 26-C) 111.35 (31-C, 38-C) 118.27 (13-C, 30-C) 119.79 (15-C, 28-C) 128.65 (14-C, 29-C) 141.71 (16-C, 27-C) 159.69 (12-C, 1-C). MALDI-TOF, m/z:=549.2 $[M+Na]^+$; 565.5 $[M+K]^+$; 658.6 $[M+Cs]^+$. $C_{30}H_{38}O_8$ requires: C, 68.42; H, 7.28%; found: C, 68.47; H, 7.33%

2,5,8,11,18,25,32,35,38,41,48,55,62,67,70,75hexadecaoxaundecacyclo[55.3.2^{17,20}.2^{20,23}.2^{23,26}.2^{47,50}.2^{50,53}.2^{53,56}.1.^{1,57}.1^{12,16}.1^{27,31}.1.^{42,46}]hexaheptaconta-12,14,27,29,42,44,57, 59,61,68,69,76(1)-dodecaene (4b). White solid, mp 183-184 ºC, column chromatography, (toluene/acetone/ethyl acetate = 4/1/0.5; R_f=0.21) 14% yield. δ_H (600 MHz, Tol-*d*8) 1.22 (t, *J*=6.6 Hz, 8H, 21-H, 65-H, 51-H, 73-H), 1.76 (t, *J*=6.6 Hz, 8H, 22-H, 64-H, 52-H, 72-H), 3.56 (d, *J*=11.4 Hz, 8H, 19-H_{ax}, 24-H_{ax}, 49-H_{ax}, 54-H_{ax}, 63-H_{ax}, 66-H_{ax}, 71-H_{ax}, 74-H_{ax}), 3.70 (s, 8H, 6-H, 7-H, 36-H, 37-H), 3.82 (t, *J*=4.8 Hz, 8H, 4-H, 9-H, 34-H, 39-H), 3.99 (d, *J*=11.4 Hz, 8H, 19-H_{eq}, 24-H_{eq}, 49-H_{eq}, 54-H_{eq}, 63-H_{eq}, 66-H_{eq}, 71-H_{eq}, 74-H_{eq}), 4.10 (t, *J*=4.8 Hz, 8H, 3-H, 10-H, 33-H, 40-H), 5.32 (s, 4H, 17-H, 26-H, 47-H, 56-H), 6.85 (ddd, *J*=1.8, 2.4, 7.2 Hz, 4H, 13-H, 30-H, 43-H, 60-H), 7.01 (d, *J*=7.8 Hz, 4H, 15-H, 28-H, 45-H, 58-H), 7.04 (overlapped peaks, 4H, 61-H, 68-H, 69-H, 76-H), 7.21 (t, *J*=7.8 Hz, 4H, 14-H, 29-H, 44-H, 59-H); δ_C (150 MHz, Tol-*d*8) 25.47, 26.92 (21-C, 22-C, 51-C, 52-C, 64-C, 65-C, 72-C, 73-C), 32.91 (20-C, 23-C, 50-C, 53-C), 67.69 (3-C, 10-C, 33-C, 40-C), 70.05 (4-C, 9-C, 34-C, 39-C), 71.20 (6-C, 7-C, 36-C, 37-C), 75.48 (19-C, 24-C, 49-C, 54-C, 63-C, 66-C, 71-C, 74-C), 102.16 (17-C, 26-C, 47-C, 56-C), 112.27 (61-C, 68-C, 69-C, 76-C), 115.86 (13-C, 30-C, 43-C, 60-C), 118.88 (15-C, 28-C, 45-C, 58-C), 129.58 (14-C, 29-C, 44-C, 59-C), 140.03 (16-C, 27-C, 46-C, 57-C), 159.08 (12-C, 31-C, 42-C, 1-C). MALDI-TOF, m/z=1075.5 $[M+Na]^+$, 1091.5 $[M+K]^+$. $C_{60}H_{76}O_{16}$ requires: C, 68.42; H, 7.28%; found: C, 68.55; H, 7.39%.

2,5,8,11,14,21,28,35,40-nonaoxahexacyclo[28.3.2^{20,23}.2^{23,26}.2^{26,29}.1^{1,30}.1^{15,19}]hentetraconta-1(41),15,17,19(34), 30(31),32-hexaene (5a). White solid, mp 182-183 ºC, column chromatography, (dichloromethane/ethylacetate =3/7; R_f=0.35) 16.0% yield. δ_H (600 MHz, C_6D_6) 0.5 (s, 4H, 24-H, 25-H), 1.92 (s, 4H, 37-H, 38-H), 3.15 (d, *J*=10.8 Hz, 4H, 22-H_{ax}, 27-H_{ax}, 36-H_{ax}, 39-H_{ax}), 3.38 (s, 8H, 6-H, 7-H, 9-H, 10-H), 3.51 (t, *J*=6 Hz, 4H, 4-H, 12-H), 3.73 (d, *J*=10.8 Hz, 4H, 22-H_{eq}, 27-H_{eq}, 36-H_{eq}, 39-H_{eq}), 3.91 (t, *J*=6 Hz, 4H, 3-H, 13-H), 5.35 (s, 2H, 20-H, 29-H), 6.93 (dd, *J*=8.4, 10.8 Hz, 2H, 16-H, 33-H), 6.94 (d, *J*=6.6 Hz, 2H, 18-H, 31-H), 7.08 (t, *J*=7.8 Hz, 2H, 17-H, 32-H), 7.71 (d, *J*=1.2 Hz, 2H, 34-H, 41-H); δ_C (150 MHz, C_6D_6) 26.24 (37-C, 38-C), 26.44 (24-C, 25-C), 33.38 (23-C, 26-C), 67.61 (3-C, 13-C), 70.29 (4-C, 12-C), 71.53, 71.74 (6-C, 7-C, 9-C, 10-C), 75.39 (22-C, 27-C, 36-C, 39-C), 103.14 (20-C, 29-C), 112.28 (34-C, 41-C), 117.93 (16-C, 33-C), 120.58 (18-C, 31-C), 129.61 (17-C, 32-C), 141.97 (19-C, 30-C), 160.39 (1-C, 15-C). FAB, m/z=571.0 $[M+H]^+$. $C_{30}H_{38}O_8$ requires: C, 67.35; H, 7.42%; found: C, 67.55; H, 7.61%.

2,5,8,11,14,17,24,31,38,43-decaoxahexacyclo[31.3.2^{23,26}.2^{26,29}.2^{29,32}.1^{1,33}.1^{18,22}]tetratetraconta-1(44), 18,20,22 (37),33,35-hexaene (6a). White solid, mp 167-168 ºC, column chromatography, (toluene/acetone/ethylacetate =4/1/0.2; R_f=0.26) 14.0% yield. δ_H (600 MHz, $CDCl_3$) 1.14 (s, 4H, 40-H, 41-H), 2.09 (s, 4H, 27-H, 28-H), 3.59 (d, *J*=12 Hz, 4H, 25-H_{ax}, 30-H_{ax}, 42-H_{ax}, 39-H_{ax}), 3.70 (s, 4H, 9-H, 10-H), 3.70-3.72 (overlapped peaks, 4H, 7-H, 12-H), 3.74-3.76 (overlapped peaks, 4H, 6-H, 13-H), 3.88 (t, *J*=5.4 Hz, 4H, 4-H, 15-H), 4.07 (d, *J*=12 Hz, 4H, 25-H_{eq}, 30-H_{eq}, 42-H_{eq}, 39-H_{eq}), 4.19 (t, *J*=5.4 Hz, 4H, 3-H, 16-H), 5.40 (s, 2H, 23-H, 32-H), 6.90-6.91 (overlapped peaks, 2H, 21-H, 34-H), 6.91-6.92 (overlapped peaks, 2H, 19-H, 36-H) 7.24 (t, *J*=7.8 Hz, 2H, 20-H, 35-H) 7.29 (dd, *J*=1.8, 2.4 Hz, 2H, 37-H, 44-H); δ_C (150 MHz, $CDCl_3$) 25.86 (27-C, 28-C), 26.40 (40-C, 41-C), 33.01 (26-C, 29-C), 67.45 (3-C, 16-C), 69.93 (4-C, 15-C), 71.02, 71.04, 71.08(6-C, 7-C, 9-C, 10-C, 12-C, 13-C), 75.41 (25-C, 30-C, 39-C, 42-C), 102.43 (23-C, 32-C) 111.19 (37-C, 44-C) 116.60 (19-C, 36-C) 119.91 (21-C, 34-C) 129.31 (20-C, 35-C) 140.07 (22-C, 33-C), 159.43 (1-C, 18-C). MALDI-TOF, m/z=637.3 $[M+Na]^+$, 653.3

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$[M+K]^+$. $C_{35}H_{49}O_{10}$ requires: C, 66.75; H, 7.84%; found: C, 66.56; H, 7.69%.

2,5,8,11,14,17,20,27,34,41,46-undecaoxahexacyclo [34.3.1^{21,25}.2^{26,29}.2^{29,32}.2^{32,35}1^{1,36}]heptatetraconta-1 (47),21,23, 25(40),36,38-hexaena (7a). White solid, mp123-123.5 ºC, column chromatography, (dichloromethane/ethylacetate =3/2; R_f=0.18) 9.0% yield. δ_H (600 MHz, C_6D_6) 0.48 (s, 4H, 30-H, 31-H), 1.89 (s, 4H, 43-H, 44-H), 3.15 (d, *J*=11.1 Hz, 4H, 28-H_{ax}, 33-H_{ax}, 42-H_{ax}, 45-H_{ax}) 3.42 (overlapped peaks, 16H, 6-H, 7-H, 9-H, 10-H, 12-H, 13-H, 15-H, 16-H), 3.50 (t, *J*=4.8 Hz, 4H, 4-H, 18-H), 3.75 (d, *J*=11.1 Hz, 4H, 28-H_{eq}, 33-H_{eq}, 42-H_{eq}, 45-H_{eq}) 3.83 (t, *J*=4.8 Hz, 4H, 3-H, 19-H,) 5.34 (s, 2H, 26-H, 35-H), 6.85 (ddd, *J*=1.2, 3, 2.4 Hz, 2H, 22-H, 39-H), 7.04 (d, *J*=7.8 Hz, 2H, 24-H, 37-H), 7.1 (t, *J*=7.8 Hz, 2H, 23-H, 38-H), 7.69 (dd, *J*=1.2, 2.4 Hz, 2H, 40-H, 47-H); δ_C (150 MHz, C_6D_6) 26.37 (43-C, 44-C), 26.73 (30-C, 31-C), 33.19 (29-C, 32-C), 67.14 (3-C, 19-C), 70.48 (4-C, 18-C), 71.61, 71.63 (6-C, 7-C, 9-C, 10-C, 12-C, 13-C, 15-C, 16-C), 75.66 (28-C, 33-C, 42-C, 45-C), 103.01 (26-C, 35-C), 112.89 (40-C, 47-C), 116.51 (22-C, 39-C), 120.47 (24-C, 37-C), 129.69 (23-C, 38-C), 141.73 (25-C, 36-C), 160.37 (1-C, 21-C). MALDI-TOF, m/z=681.3 $[M+Na]^+$; 697.5 $[M+K]^+$. $C_{36}H_{50}O_{11}$ requires: C, 65.64; H, 7.65%; found: C, 65.82; H, 7.53%.

2,5,8,11,14,17,20,27,34,41,44,47,50,53,56,59,66,73, 80,85,88,93-docosaoxaundecacyclo[73.3.2^{26,29}. 2^{29,32}.2^{32,35}.2^{65,68}.2^{68,71}.2^{71,74}.1^{1,75}.1^{21,25}.1^{36,40}.1^{60,64}]-tetranonaconta-21,23,36,38,60,62,75,77,1(94),79, 86,87-dodecaene (7b; *anti -anti*). White solid, mp 95-96 ºC; rt = 23.45 min. (HPLC); 22.0% yield. δ_H (400 MHz, CD_2Cl_2) 1.23 (t, *J*=6.8 Hz, 8H, 30-H, 83-H, 69-H, 91-H), 1.76 (t, *J*=6.8 Hz, 8H, 31-H, 82-H, 70-H, 90-H), 3.57 (d, *J*=11.4 Hz, 8H, 28-H_{ax}, 33-H_{ax}, 67-H_{ax}, 72-H_{ax}, 81-H_{ax}, 84-H_{ax}, 89-H_{ax}, 92-H_{ax}), 3.59 (s, 16H, 9-H, 10-H, 12-H, 13-H, 48-H, 49-H, 51-H, 52-H), 3.61-3.62 (overlapped peaks, 8H, 7-H, 15-H, 46-H, 54-H), 3.65-3.67 (overlapped peaks, 8H, 6-H, 16-H, 45-H, 55-H), 3.80 (t, *J*=4.8 Hz, 8H, 4-H, 18-H, 43-H, 57-H), 3.99 (d, *J*=11.4 Hz, 8H, 28-H_{eq}, 33-H_{eq}, 67-H_{eq}, 72-H_{eq}, 81-H_{eq}, 84-H_{eq}, 89-H_{eq}, 92-H_{eq}), 4.11 (t, *J*=4.8 Hz, 8H, 3-H, 19-H, 42-H, 58-H), 5.34 (s, 4H, 26-H, 35-H, 65-H, 74-H), 6.88 (ddd, *J*=2.4, 4.2, 8 Hz, 4H, 22-H, 39-H, 61-H, 78-H), 7.02 (overlapped peaks, 4H, 24-H, 37-H, 63-H, 76-H), 7.04 (overlapped peaks, 4H, 79-H, 86-H, 87-H, 94-H), 7.25 (t, *J*=8 Hz, 4H, 23-H, 38-H, 62-H, 77-H); δ_C (100 MHz, CD_2Cl_2) 25.76, 27.16 (30-C, 31-C, 69-C, 70-C, 83-C, 82-C, 90-C, 91-C), 33.17 (29-C, 32-C, 68-C, 71-C), 68.10 (3-C, 19-C, 42-C, 58-C), 70.21 (4-C, 18-C, 43-C, 57-C), 71.13 (7-C, 9-C, 10-C, 12-C, 13-C, 15-C, 46-C, 48-C, 49-C, 51-C, 52-C, 54-C), 71.34 (6-C, 16-C, 45-C, 55-C), 75.73 (28-C, 33-C, 72-C, 67-C, 81-C, 84-C, 89-C, 92-C), 102.35 (26-C, 35-C, 65-C, 74-C), 112.83 (79-C, 86-C, 87-C, 94-C), 115.55 (22-C, 39-C, 61-C, 78-C), 119.25 (24-C, 37-C, 63-C, 76-C), 129.72 (23-C, 38-C, 62-C, 77-C), 140.97 (25-C, 36-C, 64-C, 75-C), 159.37 (1-C, 21-C, 40-C, 60-C). MS (ESI): 1339.8 $[M+Na]^+$, 1355.2 $[M+K]^+$. $C_{72}H_{100}O_{22}$ requires: C, 65.63; H, 7.64%; found: C, 65.48; H, 7.70%.

2,5,8,11,14,17,20,27,34,41,44,47,50,53,56,59,66,73, 80,85,88,93-docosaoxaundecacyclo[73.3.2^{26,29}. 2^{29,32}.2^{32,35}.2^{65,68}.2^{68,71}.2^{71,74}.1^{1,75}.1^{21,25}.1^{36,40}.1^{60,64}]-tetranonaconta-21,23,36,38,60,62,75,77,1(94),79, 86,87-dodecaene (7b'). White solid, mp 88-89 ºC, rt = 22.03 min. (HPLC); 21.0% yield. δ_H (400 MHz,THF-*d*8) 1.07 (s, 4H, 30-H, 31-H),1.20 (t, *J*=6.8 Hz, 69-H, 91-H), 1.76 (t, *J*=6.8 Hz, 70-H, 90-H) 1.89 (s, 4H, 82-H, 83-H), 3.51 (t, *J*=11.2 Hz, 8H, 28-H_{ax}, 33-H_{ax}, 84-H_{ax}, 81-H_{ax}, 89-H_{ax}, 92-H_{ax}, 67-H_{ax}, 72-H_{ax}), 3.54-3.60 (overlapped peaks, 32H, 6-H, 7-H, 9-H,10-H, 12-H, 13-H, 15-H, 16-H, 45-H,46-H, 48-H, 49-H, 51-H, 52-H, 54-H, 55-H), 3.73-3.77 (overlapped peaks, 8H, 4-H, 18-H, 43-H, 57-H), 4.00 (t, *J*=11.2 Hz, 8H, 28-H_{eq},33-H_{eq}, 84-H_{eq}, 81-H_{eq}, 89-H_{eq}, 92-H_{eq}, 67-H_{eq}, 72-H_{eq}), 4.04-4.07 (overlapped peaks, 8H, 3-H, 19-H, 42-H, 58-H), 5.33 (s, 4H, 26-H, 35-H, 65-H, 74-H), 6.82-6.85 (overlapped peaks, 4H, 22-H, 39-H, 61-H, 78-H), 6.94-7.00 (overlapped peaks, 4H, 24-H, 37-H, 63-H, 76-H), 7.03-7.05 (overlapped peaks, 79-H, 86-H, 87-H, 94-H), 7.14-7.19 (overlapped peaks, 23-H, 38-H, 62-H, 77-H); δC (100 MHz,THF-d8) 33.50, 33.57 (9-C, 10-C, 12-C, 13-C, 48-C, 49-C, 51-C, 52-C), 68.55 (3-C, 19-C, 42-C, 58-C), 70.73 (4-C, 18-C, 43-C, 57-C), 71.73, 71.76, 71.86 (6-C, 7-C, 15-C, 16-C, 45-C, 46-C, 54-C, 55-C), 75.99 (28-C, 33-C, 81-C, 84-C, 89-C, 67-C, 72-C, 92-C), 102.76 (26-C, 35-C, 65-C, 74-C), 113.6 (79-C, 86-C, 87-C, 94-C), 115.4 (22-C, 39-C, 61-C, 78-C), 119.53 (24-C, 37-C, 63-C, 76-C), 129.55 (23-C, 38-C, 62-C, 77-C), 141.87 (25-C, 36-C, 64-C, 75-C), 160.03 (21-C, 40-C, 60-C, 1-C). MS (ESI): 1339.9 $[M+Na]^+$, 1355.2 $[M+K]^+$. $C_{72}H_{100}O_{22}$ requires: C, 65.63; H, 7.64%; found: C, 65.77; H, 7.76%.

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REFERENCES

(1) Zhang, X. X.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev.* **1997**, *97*, 3313.
(2) Izatt, R. M.; Pawlak, K.; Bradshaw, J.S. *Chem. Rev.* **1991**, *91*, 1721.
(3) Klein, E.; Crump, M. P.; Davis, A. P. *Angew. Chem. Int. Ed.* **2005**, *44*, 298.

For Peer Review Only

(4) Matsumoto, M.; Hamaoka, K; Takashima, Y; Yokokawa, M.; Yamada, K.; Watanabe, N.; Ijuin, H. K. *Chem. Commun.* **2005**, 808.
(5) Huang, F.; Guzei, I. A.; Jones, J. W.; Gibson H. W. *Chem. Commun.* **2005**, 1693.
(6) Huang, F.; Zhou, L.; Jones, J. W.; Gibson, H. W.; Ashraf-Khorassani, M. Chem. Commun. **2004**, 2670.
(7) Ilioudis, C. A.; Tocher, D. A.; Steed, J. W. *J. Am. Chem. Soc*. **2004**, *126* , 12395.
(8) Gallant, A. J.; Patrick, B. O.; MacLachlan; M. J. *J. Org. Chem.* **2004**, 69, 8739.
(9) Galaup, C.; Couchet, J. M.; Bedel, S.; Tisnès, P.; Picard C. J. Org. Chem. **2005**, *70*, 2274.
(10) Player, T. N.; Shinoda, S.; Tsukube, H. *Org. Biomol. Chem.* **2005**, *3*, 1615.
(11) García, F.; Goodman, J. M.; Kowenicki, R. A.; Kuzu, I.; McPartlin, M.; Silva, M. A.; Riera, L.; Woods, A. D.; Wright D. S. *Chem. Eur. J.* **2004**, *10*, 6066.
(12) Rebek, J. Jr. *Angew. Chem. Int. Ed.* **2005**, *44*, 2068.
(13) Koskela, S. J. M.; Fyles, T. M.; James, T. D. *Chem. Commun.* **2005**, 945.
(14) Huang, F.; Gibson, H. W. *Chem. Commun.* **2005**, 1696.
(15) Mahoney, J. M.; Stucker, K. A.; Jiang, H.; Carmichael, I.; Brinkmann, N. R.; Beatty, A. M.; Noll, B. C.; Smith, B. D. *J. Am. Chem. Soc*. **2005**, *127*, 2922.
(16) Li, Z. B.; Lin, J.; Zhang, H. C.; Sabat, M.; Hyacinth, M.; Pu, L. *J. Org. Chem.* **2004**, *69*, 6284.
(17) Nakahara, Y.; Kida, T.; Nakatsuji, Y.; Akashi, M. *Org. Biomol. Chem.* **2005**, *3*, 1787.
(18) Kim, S. K.; Singh, N. J.; Kim, S. J.; Swamy, K. M. K.; Kim, S. H.;Lee, K. H.; Kimb, K. S.; Yoona, J. *Tetrahedron* **2005**, *61,* 4545.
(19) Höger, S.; *Chem. Eur. J.* **2004**, *10*, 1320.
(20) Bag, B.; Bharadwaj, P. K *Chem. Commun.* **2005**, 513.
(21) Sly, J.; Kasák, P.; Nadal, E. G.; Rovira, C.; Górriz, L.; Thordarson, P.; Amabilino, D. B.; Rowan, A. E.; Nolte, R. J. M. *Chem. Commun.* **2005**, 1255.
(22) Tönshoff, C.; Merz, K.; Bucher, G. *Org. Biomol. Chem.* **2005**, *3*, 303.
(23) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*, Wiley&Sons, New York, **2000**, p. 87.
(24) Blankenstein, J.; Zhu, J. *Eur. J. Org. Chem*. **2005**, 1949.
(25) Diederich, F.; Stang, P.J. *Templated Organic Synthesis*, Wiley-VCH, Weinheim, Germany, **2000**, p. 4.
(26) Hiraga, H.; Morozumi, T.; Nakamura, H. *Eur. J. Org. Chem* **2004**, 4680.
(27) Jaunzems, J.; Oelze, B.; Kirschning, A. *Org. Biomol. Chem.* **2004**, *2*, 3448.
(28) Robertson, J.; Meo, P.; Dallimore, J. W. P.; Doyle, B. M.; Hoarau, C.; *Org. Lett.,* **2004**, *6*, 3861.
(29) Piatek, P.; Gruza, M. M.; Jurczak, J. *Tetrahedron: Asymmetry* **2001**, *12*, 1763.
(30) Wenzel, T. J.; Thurston, J. E.; Sek, D. C.; Joly, J. P. *Tetrahedron: Asymmetry* **2001**, *12*, 1125.
(31) Bakó, T.; Bakó, P.; Szöllõsy, Á.; Czugler, M.; Keglevich, G.; Tõke, L. *Tetrahedron: Asymmetry*, **2002**, *13*, 203.
(32) Wybrow, R.A.J.; Johnson, L.A.; Auffray, B.; Moran, W.J.; Adams, H.; Harrity, J.P.A. *Tetrahedron Lett.,* **2002**, *43*, 7851.
(33) Ito, T.; Tokuyasu, T.; Masuyama, A.; Nojima, M.; McCullough, K.J. *Tetrahedron*, **2003**, *59*, 525.
(34) Garcia, C.; Pointud, Y.; Jeminet, G.; Dugat, D. *Tetrahedron Lett*. **1999**, *40*, 4933.
(35) Garcia, C.; Guyot, J.; Jeminet, G.; Leize-Wagner, E.; Nierengarten, H.; Van Dorsselaer, A. *Tetrahedron Lett*. **1999**, *40*, 4997.
(36) Bakó, P.; Novák, T.; Ludányi, K.; Pete, B.; Tõke, L.; Keglevich, G. *Tetrahedron: Asymmetry* **1999**, *10*, 2373.
(37) Galan, M. C.; Venot, A. P.; Glushka, J.; Imberty, A.; Boons, G. J. *J. Am. Chem. Soc*. **2002**, *124*, 5964.
(38) Grosu, I.; Bogdan, E.; Plé, G.; Toupet, L.; Ramondenc, Y.; Condamine, E.; Peulon-Agasse, V.; Balog, M. *Eur. J. Org. Chem.* **2003**, 3153.
(39) Balog, M.; Grosu, I.; Plé, G.; Ramondenc, Y.; Toupet, L.; Condamine, E.; Lange, C.; Loutelier-Agasse, C.; Peulon-Agasse, V.; Bogdan, E. *Tetrahedron* **2004**, *60*, 4789.
(40) Grosu, I. ; Mager, S. ; Plé, G.; Mesaros, E. *Tetrahedron* **1996**, *52*, 12783.
(41) Cismas, C.; Terec, A.; Mager, S.; Grosu, I. *Curr. Org. Chem.,* **2005***, 9*,1287.
(42) Feuerbacher, N; Vögtle, F.; Windscheidt, J.; Poetsch, E.; Nieger, M. *Synthesis*, **1999**, 117.
(43) Campbell, T. W.; Foldi,V. S. *J. Org. Chem.* **1961**, *26*, 4654.
(44) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds,* Wiley&Sons, New York, **2004**, p. 1178.
(45) Nonius,. *KappaCCD Software*. Nonius BV, Delft, **1999**, The Netherlands
(46) Otwinowski, Z.; Minor, W. *Processing of X-ray Diffraction Data Collected in Oscillation Mode*, in *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by Carter, C. W.; Sweet, R. M. *Academic Press*, London, **1997**, p. 307.
(47) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.G.G.; Polidori, G.; Spagna R., *Sir97: a new tool for crystal structure determination and refinement. Jr of Applied Crystallography* **1998**, *31*, 74.
(48) Sheldrick, G.M. *SHELX97. Program for the Refinement of Crystal Structures*, Univ. of Göttingen, **1997**, Germany.
(49) *International Tables for X-ray Crystallography* Vol.C. Wilson A.J.C. (Editor) Kluwer Academic Publishers, **1992**, Dordrecht, Germany
(50) Spek, A.L. *PLATON. A multipurpose crystallographic tool,* Utrecht University, **1998**, Utrecht, The Netherlands.

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